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Omentin-1 Level in Middle Age Women with Hypothyroidism and their Relations to Risk factors of Cardiovascular Disease

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Abstract

Background Omentin-1 is fat deposition-specific adipokine that is highly and selectively expressed in visceral adipose tissue. Low circulating levels of Omentin-1 have been associated with endothelial dysfunction and cardiovascular disease. Abnormalities of lipid metabolism associated with subclinical and overt hypothyroidisms patients, low Omentin-1 level can affect risk factors for cardiovascular disease.

Objective To determine the differences in the levels of Omentin-1 in middle age women with subclinical and overt hypothyroidisms and correlate its level with parameters which considered risk factor for cardiovascular disease.

Methods Ninety middle age women divided into three groups as follows: group I consisted of 30 healthy women as a control subject, group II comprised 30 women with subclinical hypothyroidisms, group III include 30 women with overt hypothyroidisms, serum of Omentin-1, high sensitive c-reactive protein and lipid profile levels were evaluated in patients and control groups.

Results Serum omentin-1 levels were significant decreased in patients with subclinical and overt hypothyroidisms compared with control group. Significant negative correlation between omentin-1 and thyroid-stimulating hormone, high sensitive c-reactive protein, total cholesterol, atherogenic index in patients was found. Significant positive correlation was observed between Omentin-1 and high-density lipoprotein in the patients.

Conclusion we conclude that serum Omentin-1 levels were decrease in middle age women with hypothyroidism and its correlate with altering lipid profile, high levels of atherogenic index and high sensitive c-reactive protein, all of these conditions is correlated with cardiovascular disease, so Omentin-1 in hypothyroidism patients is a risk factor for cardiovascular disease, our suggestion that possible follow up serum lipid profile and omentin-1 monthly for middle age women to prevent cardiovascular disease.

Keywords Omentin-1, lipid profile, hypothyroidism disease

List of abbreviation: SHT = subclinical hypothyroidisms, OHT = overt hypothyroidisms, CVD = cardiovascular disease, OM-1 = omentin-1, TNF-α = tumor necrosis factor-α, IL-6 = interleukin-6, TSH = thyroid-stimulating hormone, TC = total cholesterol, LDL = low density lipoprotein, CAD = coronary artery disease, hsCRP = high sensitive c-reactive protein, AI = atherogenic index, BMI = body mass index, BFP = body fat percentage, ELISA = enzyme-linked immune sorbet assay, TG = Total triglyceride, VLDL = very low density lipoprotein.

Introduction

Adipose tissue secretes many adipokines including adiponectin, chemerin, leptin, resistin, retinol binding protein 4, tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) [(1)]. These adipokines play important roles in carbohydrate and lipid metabolism, homeostasis, insulin resistance, diabetes, atherosclerosis, vascular endothelial dysfunction, inflammation, and cardiovascular function [(2,3)]. Omentin, a recently identified fat deposition-specific adipokine codified by two genes (1 and 2), omentin-1 has been shown to be the major circulating isoform in human plasma [(4)].

Omentin-1 or Intelectin-1 (OM-1) is a newly identified protein (32 kDa adipokine) that is highly and selectively expressed in visceral adipose tissue and is expressed to a lesser extent in the heart, lung, and placenta [5].

Dysregulation of (OM-1) secretion is thought to play a role in the pathophysiology of endothelial dysfunction, and cardiovascular disease [6]. (OM-1) may act as an endocrine factor affecting muscles [7].

In clinical studies, circulating (OM-1) concentrations have been shown to be decreased in patients with obesity, impaired glucose regulation, polycystic ovary syndrome, type 1 diabetes, and type 2 diabetes [8-11].

Low circulating levels of (OM-1) have also been associated with endothelial dysfunction and cardiovascular disease [12-17].

Hypothyroidism is caused either by inadequate function of the gland itself (primary hypothyroidism) or by not enough stimulation by thyroid-stimulating hormone (TSH), central hypothyroidism [18,19].

In overt primary hypothyroidism (OHT), TSH levels are high; T4 and T3 levels are low. TSH usually rises after T4 and T3 levels drop.

Subclinical hypothyroidism (SHT) is a milder form of hypothyroidism characterized by an elevated serum TSH level, but with a normal serum free thyroxine level [20]. Hypothyroid patients have increased levels of total cholesterol (TC) and low-density lipoprotein (LDL). Indeed, hypo-thyroidism is a common cause of secondary dyslipidemia [21].

The abnormalities of lipid metabolism associated with (OHT) predispose to the development of atherosclerotic coronary artery disease (CAD) [22]. Moreover, hypothyroidism can adversely affect other CVD risk factors, further contributing to increasing CAD risk. Decreased thyroid function not only increases the number of LDL particles, but also promotes LDL oxidability [23].

In addition, thyroid failure is strongly associated with arterial hypertension (especially diastolic) via sympathetic and adrenal activation, and increased vascular stiffness. Subjects with (OHT) also exhibit impaired endothelial function [24].

We hypothesized that omentin-1 might be implicated in CVD in patients with (SHT and OHT) due to a possible association with inflammation endothelial function. To test the hypothesis, serum (OM-1) levels in women have (SHT and OHT) patients are measured, and compared them with healthy women subject as a control group and evaluated possible correlations with other cardiovascular risk factors such as high sensitive c-reactive protein (hsCRP), lipid profile and atherogenic index (AI).

Methods

Ninety women (age 40-60) years were enrolled in this study, blood was collected from women patients attended the Baghdad Teaching Hospital, Al-Kindy Hospital and Al-Imamain Al-Kadhemain Medical City from March 2011 to September 2012. The women were divided into three groups as follows: group I consist of 30 healthy women as a control group, group II consist of 30 OHT patients and group III consist of 30 SHT patients.

All women patients were diagnosed by physicians and other complications were excluded such as cardiovascular disease, diabetes mellitus, renal failure and hypertension. The range of body mass index (BMI) for the patients and control was 32-38 Kg/m^2 and the range of body fat percentage (BFP) was (30-39), Patients and control groups were determined the following parameters:

- TSH, T3, T4, OM-1 and high sensitive c-reactive protein (hsCRP) levels were measured by enzyme-linked immune sorbet assay (ELISA) method [25,26].
- Total cholesterol (TC) was determined using enzyme-catalyzed colorimetric method [27].
- Total triglyceride (TG) was determined using enzyme-catalyzed colorimetric method [28].
- Serum HDL was measured using Burstein separation method using HDL-C kit [29].
- By using the Friedwald equation, low density lipoprotein (LDL) = TC-[TG/5 + HDL], very low

density lipoprotein (VLDL) = TG/5, atherogenic index of plasma (AIP)= Log(TG/HDL) [30].

Statistical Analysis

Data are presented as mean ±SD using SPSS program. The differences between two groups were analyzed by t-test. *P* value less than 0.05 considered significant. Pearson's correlation coefficient was used to examine between (OM-1) and other parameters in patients groups.

Results

Table 1 shows the level of OM-1, thyroid hormones and lipid profile of the studied groups. The serum level of T3, T4, HDL and OM-1 were significantly lower in the patient than in the control group ($P < 0.05$). The serum level of T3, T4, HDL and OM-1 levels were significantly lower in OHT patients than in the SHT patients ($P < 0.05$).

The serum levels of TSH, hsCRP, TC, HDL, LDL, VLDL, and AI were significantly higher in SHT and OHT patients than in the control group ($P < 0.05$) and TG level was insignificantly higher than the control group.

The serum levels of TSH, hsCRP, TC, HDL, LDL, VLDL, AIP levels were significantly higher in OHT patients than in the SHT patients ($P < 0.05$) and TG level was insignificantly higher than the SHT patients.

Table 1. Omentin-1, thyroid functions, inflammatory markers and lipid profile in the control group and patients with subclinical and overt hypothyroidism patients.

Parameter		Groups			*P* Value		
		I	II	III	I-III	I-II	III-II
Thyroid functions	T3 (ng/mL)	1.2±0.5	0.7±0.2	0.3±0.1	s	s	s
	T4 (ng/dL)	1.7±0.7	0.9±0.34	0.5±0.12	s	s	s
	TSH (mU/L)	1.92±0.8	7.86±3.1	19.34±4.3	s	s	s
OM-1 (ng/mL)		12.3±2.2	9.7±1.4	7.8±1.1	s	s	s
hsCRP (g/L)		2.25±0.42	4.23±1.2	7.81±2.7	s	s	s
Lipid profile	TG (mg/dL)	104.5±28.3	117.3±21.2	129.6±32.8	s	ns	ns
	TC (mg/dL)	166.0±27.3	195.5±36.2	232.8±57.2	ns	s	s
	HDL (mg/dL)	44.1±9.2	36.1±15.8	30.3±12.3	s	s	s
	LDL (mg/dL)	101.0±15.9	119.7±39.6	128.6±45.7	s	s	s
	VLDL (mg/dL)	25.2±6.5	30.3±9.4	37.1±11.4	s	s	s
	AI (mg/dL)	0.34±0.1	0.55±0.13	0.8±0.14	s	s	s

OM-1 = omentin-1, TSH = thyroid-stimulating hormone, TC = total cholesterol, LDL = low density lipoprotein, hsCRP = high sensitive C-reactive protein, AI = atherogenic index, TG = Total triglyceride, VLDL = very low density lipoprotein, HDL = high-density lipoprotein, s = significant (P < 0.05), ns = not significant.

A significant negative correlation was noticed between OM-1 and TSH, hsCRP, TC and AIP in patients with SHT and OHT. A significant positive correlation was seen between OM-1 and HDL in patients with SHT and OHT. No significant positive correlation was observed between OM-1 and T3 and T4 in patients with SHT and OHT. No significant negative correlation between OM-1 TG and LDL in patients with SHT and OHT (Table 2).

Discussion

To our knowledge, the current study, is the first study exploring the serum OM-1 levels in SHT and OHT patients, we sought to determine the relationship between circulating OM-1 levels and T3, T4, TSH, lipid profile and some inflammation in patients groups. AI and HDL cholesterol was found to be a significant correlate of plasma OM-1 concentrations in the entire study cohorts; these data demonstrate that omentin-1 is associated with HDL cholesterol. So it seems that

OM-1 has a role in the pathogenesis of SHT and OHT and their relation to CVD. This finding is in agreement with a recent study by Vu et al (2014) which shows that OM-1 concentration play a role in the developing of CVD [31] and the correlation between HDL cholesterol and omentin-1 has been previously described in the settings of CVD [32].

Table 2. Correlation between Omentin-1 and other parameters for the patient groups

Parameter		Subclinical hyperthyroidism		Overt hyperthyroidism	
		r value	*P* value	*r* value	*P* value
Thyroid function	T3 (ng/mL)	0.01	ns	0.27	ns
	T4 (ng/dL)	0.12	ns	0.33	ns
	TSH (mU/L)	-0.41	s	-0.54	s
hsCRP(g/L)		-0.46	s	-0.63	s
Lipid profile	TG (mg/dL)	-0.21	ns	-0.32	ns
	TC (mg/dL)	-0.53	s	-0.75	s
	HDL (mg/dL)	0.55	s	0.68	s
	LDL (mg/dL)	-0.04	ns	-0.05	ns
	VLDL (mg/dL)	-0.03	ns	-0.11	ns
	AI (mg/dL)	-0.59	s	-0.66	s

OM-1 = omentin-1, TSH = thyroid-stimulating hormone, TC = total cholesterol, LDL = low density lipoprotein, hsCRP = high sensitive C-reactive protein, AI = atherogenic index, TG = Total triglyceride, VLDL = very low-density lipoprotein, HDL = high-density lipoprotein, s = significant ($P < 0.05$), ns = not significant.

Dysregulation of omentin-1 may adversely affect insulin signaling and regulation, thereby altering HDL production and then total cholesterol concentration. Although few prospective data exist for omentin-1, some studies suggest that circulating omentin-1 concentrations are associated with atherosclerosis and CAD in different patient populations [31].

Thyroid hormones are also crucial for the regulation of total energy consumption and body composition besides their roles in normal growth, development, and reproduction.

Thyroid dysfunction is associated with weight changes. A significant negative correlation between OM-1 and TSH was found in this study.

Hypothyroidisms is also associated with insulin resistance and altering HDL-c and other lipid profile [33,34].

OM-1 is discovered to have role in regulation of metabolism and body composition, it seem to regulate thermogenesis, immunity, feeding, and neuroendocrine functions.

In this study, negative correlation of OM-1 with hsCRP was found. OM-1 has a central role in subclinical inflammation of adipose tissue [35-37].

In SHT cases, high serum cholesterol concentration was regarded as evidence for "premyxoedema" in the absence of symptoms of hypothyroidism. How many of these patients in fact had hypothyroidism is not known.

While there is no doubt that many hypothyroid patients have abnormal serum lipid concentrations, the increased risk of CAD seen in hypothyroid patients is likely multifactorial in etiology [38].

In conclusion, SHT patients have obesity, altered lipid profile and high AI and hsCRP levels; all of these conditions are correlated with CVD.

Serum OM-1 levels was decreased in hypothyroidism patients and is correlated with previous parameters, so low OM-1 level is a risk factor for CVD in hypothyroid patients.

We recommend monthly follow up by serum lipid profile for middle age women. OM-1 can be used therapeutically for better management of SHT and OHT to prevent development of CVD.

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Conflict of interest

The author declares that they have no competing interests.

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